Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

OSTEOMYELITIS

Although osteomyelitis of the jaw usually results from odontogenic (especially periapical) infection, open fracture of the jaw with delayed treatment also represents a significant inciting event. Predisposing conditions that affect host resistance and may play a role in the development of osteomyelitis of the jaw include diabetes mellitus, agranulocytosis, leukemia, sickle-cell disease, fibrous dysplasia, and Paget disease.[34,35]

Most instances of osteomyelitis of the jaw are caused by microaerophilic viridans streptococci, anaerobic streptococci, and other anaerobes, including *Peptostreptococcus*, *Fusobacterium,* and *Bacteroides* species. Only occasional cases are caused by *Staphylococcus aureus,* which is generally associated with breaks in the skin. Gram-negative organisms can also be involved, including *Salmonella* in patients with sickle-cell anemia.[35] Specific forms of disease are caused by *Actinomyces israelii, Treponema pallidum,* and nontuberculous mycobacteria.

Mandibular Osteomyelitis

The mandible is involved more often by osteomyelitis than the maxilla because of the relatively poorer blood supply, which is limited to one major vessel and the periosteal circulation. Clinical features include fever, facial swelling, jaw pain, and generally a carious or discolored tooth. Mental nerve paresthesia may be present early in the course. Management of acute suppurative osteomyelitis of the mandible is similar, in most respects, to that of acute osteomyelitis of any bone. If the infection began as a periapical dental abscess, the involved tooth should be removed as soon as possible to allow for drainage and to provide material for culture. Treatment is given for a minimum of 4 weeks. Actinomycosis is particularly challenging to manage. Amoxicillin (chosen for pharmacodynamic and antimicrobial activity) plus probenecid is usually given for 1 year or more. Relapses can occur year(s) later. Surgical debridement may be necessary to affect cure if sequestrum or involucrum is present.[36]

Infantile Maxillary Osteomyelitis

Osteomyelitis of the jaw in the neonate is rare but can have serious sequelae. It most commonly involves the maxilla and is thought to arise from neonatal trauma to oral tissues, from hematogenous spread from skin, middle ear, or mastoid, or from an infected maternal nipple. The infant manifests facial cellulitis centered on the orbit. Fever, irritability, anorexia, and dehydration in association with palpebral edema and conjunctivitis can be seen in association with purulent discharge from the nose or inner canthus. Examination of the mouth reveals swelling of the maxilla extending to both the buccal and palatal regions, with fluctuance and fistula formation often present. *Staphylococcus aureus* is the most common cause. Aggressive treatment is necessary to prevent permanent optic damage, neurologic complication, loss of tooth buds and bone, and extension to the dural sinuses.

Garré Osteomyelitis

Garré sclerosing osteomyelitis is a chronic, nonsuppurative, sclerosing osteomyelitis.[37] It is characterized by a localized, hard, nontender swelling of the mandible. It is commonly associated with a carious tooth, usually a lower first molar. Frequently, there is history of a past toothache, recent dental extraction, or infection of a flap of tissue over an erupting tooth. Radiographs show a focal area of calcified proliferation of bone that is smooth and often has a laminated or onion-peel appearance (a periosteal response to low-grade stimulus such as a dental infection). It resembles infantile cortical hyperostosis (Caffey disease), osteosarcoma, and Ewing sarcoma. Biopsy is performed to exclude neoplasm if regression does not occur after extraction of the involved tooth. Antibiotic therapy is not necessary.

CHAPTER 28

The Common Cold

Diane E. Pappas and J. Owen Hendley

The common cold, also known as upper respiratory tract infection (URI), is an acute, self-limited viral infection of the upper airway that may involve the lower respiratory tract as well. The characteristic symptom complex consisting of rhinorrhea, nasal congestion, and sore or scratchy throat is familiar to all adults. Colds are the most common cause of human illness and are responsible for significant absenteeism from school and work. Children are especially susceptible because: (1) they have not yet acquired immunity to many of the viruses; (2) they have poor personal hygiene practices; and (3) they have frequent close contact with other children who are excreting virus.

ETIOLOGY

Colds are common because some of the causative viruses do not produce lasting immunity after infection and some viruses have numerous serotypes (Table 28-1). Cold viruses that do not produce lasting immunity include respiratory syncytial virus (RSV), parainfluenza viruses, and coronaviruses. Cold viruses that have numerous serotypes but produce lasting serotype-specific immunity after infection include rhinoviruses, adenoviruses, influenza viruses, and enteroviruses.[1]

Rhinoviruses (*rhino,* nose), with at least 100 serotypes, are the most common cause of URIs in children and adults. At least 50% of colds in adults are caused by rhinovirus. Other viruses that cause URIs are coronaviruses (*corona,* crown), RSV, human metapneumovirus, influenza virus, parainfluenza virus, adenovirus, echoviruses, and coxsackieviruses A and B. Some of these viruses cause characteristic syndromes; for example, RSV causes bronchiolitis in children 2 years or younger, influenza viruses cause febrile respiratory illness with severe lower respiratory tract involvement, adenoviruses cause pharyngoconjunctival fever, parainfluenza viruses cause croup in young children, and enteroviruses cause a variety of illnesses, including aseptic meningitis and herpangina.

TABLE 28-1. Immunity to Common Cold Viruses

Virus	No of Serotypes
LONG-LASTING IMMUNITY NOT PRODUCED BY INFECTION (REPEATED INFECTION WITH SAME SEROTYPE USUAL)	
Respiratory syncytial virus (RSV)	1
Parainfluenza virus	4
Coronavirus	2
IMMUNITY PRODUCED BY INFECTION (REINFECTION WITH SAME SEROTYPE UNCOMMON)	
Rhinovirus	> 100
Adenovirus	≥ 33
Influenza	3[a]
Echovirus	31
Coxsackievirus group A	3
Coxsackievirus group B	6

[a]Type A subtypes change.
Modified from Hendley JO. Immunology of viral colds. In: Veldman JE, McCabe BF, Huizing EH, et al. (eds) Immunobiology, Autoimmunity, Transplantation in Otorhinolaryngology. Amsterdam, Kugler Publications, 1985, pp 257–260.

EPIDEMIOLOGY

In temperate climates in the northern hemisphere, the predictable yearly epidemic of colds begins in September and continues unabated until spring. This sustained epidemic curve is a result of successive waves of different respiratory viruses moving through the community (Figure 28-1). The epidemic begins with a sharp rise in the frequency of rhinovirus infections in September (after children return to school), which is followed by parainfluenza viruses in October and November. RSV and coronaviruses circulate during the winter months, whereas infection due to influenza virus peaks in the late winter. The epidemic finally ends with a small resurgence of rhinovirus infections in the spring. Adenovirus infection occurs at a constant rate throughout the cold season.[2]

The frequency of colds varies with age. A 10-year study of families with children who did not attend a childcare facility showed that the peak incidence of colds occurs in preschool children 1 to 5 years old, with a frequency of 7.4 to 8.3 colds per year. Infants younger than 1 year averaged 6.7 colds per year, and teenagers averaged about 4.5 colds per year. Mothers and fathers experienced about 4 colds per year.[3] With the greater exposure of children to other preschool children in childcare facilities, the frequency of colds in children younger than 6 years has increased. Thus, the typical preschool child experiences at least one URI per month throughout the cold season.

Viral transmission occurs primarily in the home setting, although the exact mechanism of spread has not been clearly established. Colds can be spread by: (1) small-particle (< 5 μm in diameter) aerosol, which infects when inhaled; or (2) large-particle (> 10 μm in diameter) droplets, which infect by landing on nasal or conjunctival mucosa; or (3) direct transfer via hand-to-hand contact.[4] Small-particle aerosol is an effective method of transfer for influenza virus[5] and coronavirus[6] but not for RSV.[7] Rhinoviruses are most likely spread by large-particle droplets or direct transfer. Rhinoviruses can survive as long as 2 hours on human hands and up to several days on other surfaces. Studies in young adults have shown that infected individuals commonly have rhinovirus on their hands, which can be efficiently transferred to the hands of uninfected individuals during brief contact; infection then results when the uninfected person transfers the virus from the hands on to his or her nasal or conjunctival mucosa. Sneezing and coughing are ineffective modes of rhinovirus transmission.[8] Inoculation of the oral mucosa with rhinovirus[9] or RSV[10] does not result in infection.

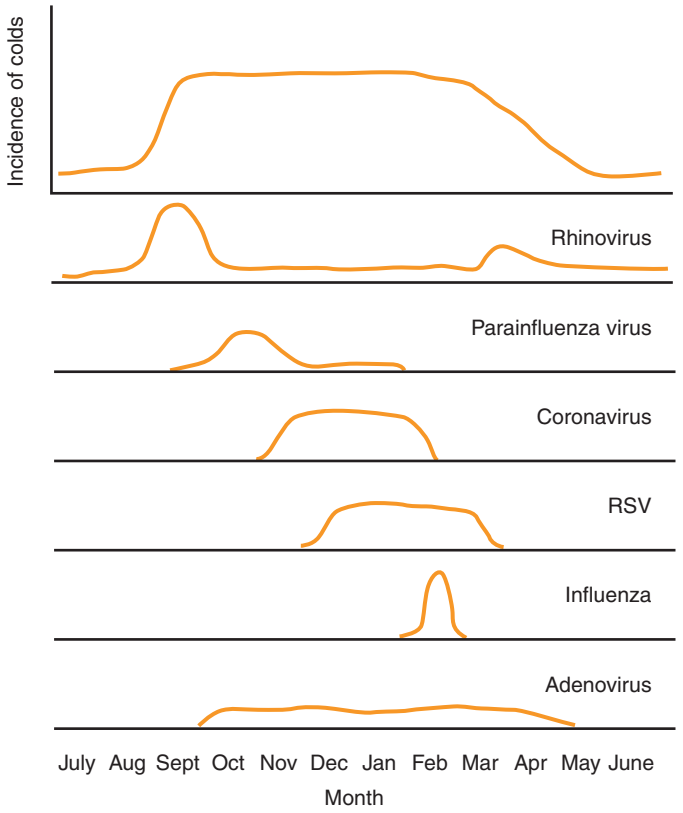

Figure 28-1. Schematic diagram of the incidence of colds and frequency of causative viruses. RSV, respiratory syncytial virus. (Redrawn from Hendley JO. The common cold. In: Goldman L, Bennett JC (eds) Cecil Textbook of Medicine, 21st ed. Philadelphia, WB Saunders, 2000, pp 1790–1793.)

PATHOGENESIS

Symptoms of the common cold do not appear to result from destruction of nasal mucosa, because nasal biopsy specimens from young adults with both natural and experimentally induced colds show intact nasal epithelium during symptomatic illness.[11,12] Study by in situ hybridization of nasal biopsy specimens obtained during rhinovirus infection indicates that replication occurs in only a small number of epithelial cells.[13,14] Furthermore, in vitro studies have shown that rhinovirus and coronavirus produce no detectable cytopathic effect when replicating in a cultured monolayer of nasal epithelial cells, whereas influenza virus A and adenovirus produce obvious damage.[15]

The symptoms of the common cold appear to result from release of cytokines and other mediators from infected nasal epithelial cells as well as from an influx of polymorphonuclear cells (PMNs). Nasal washings of volunteers experimentally infected with rhinovirus showed a 100-fold increase in PMN concentration 1 to 2 days after inoculation.[16] This influx of PMNs coincides with onset of symptoms and correlates with the presence of a colored nasal discharge.[17] A yellow or white nasal discharge may result from the higher number of PMNs, whereas the enzymatic activity of PMNs (due to myeloperoxidase and other enzymes) may cause a green nasal discharge. A potent chemoattractant for PMNs is produced by cells in culture infected with rhinovirus.[18] This chemoattractant has been identified as interleukin 8 (IL-8).[19] Elevated levels of IL-8 and other cytokines (IL-1β, IL-6) have also been demonstrated in the nasal secretions of infected individuals.[20,21] Furthermore, elevated levels of albumin and kinins (predominantly bradykinin) in nasal secretions have been shown to coincide with the onset of symptoms in experimental rhinovirus infection.[16] The elevated concentration of albumin and kinins likely results from exudation of plasma proteins due to greater vascular permeability in the nasal submucosa. The method by which viral infection initiates this vascular leak has not yet been determined. The release of kinins resulting from plasma exudation may augment the symptoms of the cold; bradykinin alone can cause rhinitis and sore throat when sprayed into the noses of uninfected individuals.[22]

The paranasal sinuses are usually involved during an uncomplicated cold caused by respiratory viruses. In one study, computed tomographic (CT) scans obtained during the acute phase of illness revealed abnormalities of one or more sinuses in 27 (87%) of 31 young adults.[23] Without antibiotic therapy, there was complete resolution or marked improvement of the sinus abnormalities in 11 (79%) of the 14 subjects in whom second CT scans were obtained 2 weeks later. It is not known whether these sinus abnormalities result from viral infection of the sinus mucosa or from impaired sinus drainage secondary to viral rhinitis. Nose-blowing can generate enough pressure to force fluid from the nasopharynx into the paranasal sinuses, suggesting that nose-blowing may force mucus containing viruses, bacteria, and inflammatory mediators into the paranasal sinuses during a cold.[24]

The middle ear can also be involved during uncomplicated colds. Studies in school-aged children have shown that two-thirds will develop abnormal middle-ear pressures within 2 weeks after onset of a cold.[25] Otitis media was not diagnosed during the study. It is not known whether the abnormal middle-ear pressures result from viral infection of the mucosa of the middle ear and eustachian tube or from viral nasopharyngitis with secondary eustachian tube dysfunction.

CLINICAL MANIFESTATIONS

Symptoms of the common cold do not vary by specific cause. In older children and adults, rhinorrhea, nasal obstruction, and sore or scratchy throat are typical. The rhinorrhea is initially clear but may become colored as the illness proceeds. Cough or sneeze may be present. Fever (> 38°C) is uncommon in adults. Other symptoms are malaise, sinus fullness, and hoarseness. Objective findings are minimal except for mild erythema of the nasal mucosa or pharynx. Symptoms resolve in 5 to 7 days.

Compared with adults, infants and preschool children with colds are more likely to have fever (≥ 38°C) and moderate enlargement of the anterior cervical nodes (Table 28-2).[1] Rhinorrhea may not be noticed until the nasal discharge becomes colored. Nasal congestion may disrupt sleep and may lead to fatigue and irritability. The illness often persists in infants and preschool children for 10 to 14 days.[26]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a cold includes allergic rhinitis, vasomotor rhinitis, intranasal foreign body, and sinusitis. A diagnosis of allergic rhinitis is suggested by a seasonal pattern of clear rhinorrhea, absence of associated fever, and family history of allergy. Possible associated conditions are asthma and eczema. Physical findings consistent with allergic rhinitis include allergic "shiners" and "nasal salute." The detection of numerous eosinophils upon microscopic examination of the nasal mucus using Hansel stain confirms the diagnosis of allergic rhinitis. A diagnosis of vasomotor rhinitis is suggested by a chronic course without fever or sore throat. The diagnosis of bacterial sinusitis is suggested by persistent rhinorrhea or cough or both for greater than 10 days.[27]

CLINICAL APPROACH

The diagnosis of a cold is based on history and physical examination; generally, laboratory tests are not useful. The rapid test for detecting RSV, influenza, parainfluenza, and adenovirus antigens in nasal secretions can be used to confirm the diagnosis. RSV, rhinovirus, influenza viruses, parainfluenza viruses, and adenoviruses can also be isolated in cell culture. Coronavirus cannot be detected reliably in cell culture, so serologic titer rise can be used for diagnosis, if necessary. Polymerase chain reaction assays for diagnosis of all the respiratory viruses are available in research laboratories and increasingly in clinical laboratories. Other methods of detection can be used but are rarely needed.

MANAGEMENT

At present, no antiviral agents are available that are effective for treatment of the common cold. Although an array of medications may be used to relieve symptoms, there is little scientific evidence to support the use of symptomatic treatments in children. Because the common cold is a self-limited illness with symptomatology that is largely subjective, a substantial placebo effect can suggest that various treatments have some efficacy. Inadequate blinding of placebo recipients in a study can make an ineffective treatment appear effective.

In adults with colds, first-generation antihistamines (i.e., chlorpheniramine) have been shown to provide modest symptomatic relief, with decreases in nasal discharge, sneezing, nose-blowing, and duration of symptoms.[28] This effect is presumably due to the anticholinergic effects of these medications. A randomized, double-blind, placebo-controlled study in preschool children with URIs showed that treatment with an antihistamine–decongestant combination (brompheniramine maleate and phenylpropanolamine hydrochloride) produced no improvement in cough, rhinorrhea, or nasal congestion, although a larger proportion of the treated children (47% versus 26%) were asleep 2 hours after treatment.[29]

Numerous decongestants, antitussives, and expectorants are available over the counter, but there is no evidence to support their use in children. A study of phenylephrine, a topical decongestant, in children 6 to 18 months old showed no decrease in nasal obstruction with its use during a URI.[30] In a study comparing placebo, dextromethorphan, and codeine for cough suppression in children 18 months to 12 years old, cough decreased in all patients within 3 days, but there was no difference in cough reduction among the three treatment groups.[31] Guaifenesin, an expectorant, has not been shown to change the volume or quality of sputum or the frequency of cough in young adults with colds.[32] Echinacea preparations, commonly believed to be effective in the treatment of the common cold, have been shown to have no effect on the prevention or treatment of rhinovirus infection.[33]

Antibiotics have no role in the treatment of uncomplicated URIs in children. Antibiotic therapy does not hasten resolution of the viral infection or reduce the likelihood of occurrence of secondary bacterial infection.[34] Antibiotics are only indicated in cases of secondary bacterial infection, such as sinusitis and acute otitis media.

Thus, supportive measures remain the mainstay of treatment of the common cold in children. Bulb suction with saline drops (about 1 teaspoon salt in 2 cups of water) may help relieve nasal congestion and remove secretions.

TABLE 28-2. Characteristics of Viral Colds in Adults and Young Children

Characteristic	Adults	Children < 6 years
Frequency	2–4 per year	One per month, September–April
Fever	Rare	Common during first 3 days
Nasal manifestations	Congestion	Colored nasal discharge
Duration of illness	5–7 days	14 days

Modified from Hendley JO. Epidemiology, pathogenesis, and treatment of the common cold. Semin Pediatr Infect Dis 1998;9:50–55.

COMPLICATIONS

The common cold usually resolves in about 10 to 14 days in infants and children. New-onset fever and earache during this period may herald the development of bacterial otitis media, which occurs in about 5% of colds in preschool children. Persistence of nasal symptoms for longer than 10 days may signify the development of a secondary bacterial sinusitis. Bacterial pneumonia is an uncommon secondary infection. For children with underlying reactive airways disease, wheezing is common during the course of a viral URI; at least 50% of asthma exacerbations in children are associated with viral infection. Children who experience more than one lower respiratory tract infection (such as croup or bronchiolitis) during their first year of life have an increased risk of asthma thereafter.[35] Other complications are epistaxis, eustachian tube dysfunction, conjunctivitis, and pharyngitis.

RECENT ADVANCES

Research now suggests that the symptoms of the common cold result from effects of inflammatory mediators released in response to the viral infection of the respiratory tract. As the determinants of this process are further elucidated, treatments may be developed that can interrupt or ameliorate release of inflammatory mediators and thus prevent or reduce the symptoms of the common cold. Vaccines are unlikely to be useful for prevention, given the large number of serotypes of some cold viruses as well as the lack of lasting immunity to others. The use of alcohol-based hand gels has been suggested as a

means of reducing secondary transmission of respiratory illnesses in the home,[36] but in one field trial, this was not shown to be effective.[37] Also, virucidal tissues have been shown to be effective in preventing viral passage and transmission, and may reduce secondary transmission by about 30%.[38,39] Until new methods are developed, prevention of the common cold is limited to avoiding self-inoculation (transfer of virus from contaminated fingers to nasal or conjunctival mucosa) by removing virus through handwashing or by killing virus with application of a virucide to the hands.

CHAPTER 29

Pharyngitis

Michael A. Gerber

Pharyngitis is an inflammation of the mucous membranes and underlying structures of the throat. Acute pharyngitis is one of the most common illnesses for which children in the United States visit primary care physicians; pediatricians make the diagnosis of acute pharyngitis, acute tonsillitis, or streptococcal sore throat more than 7 million times annually.[1]

Many viruses and bacteria can cause acute pharyngitis, either as a separate entity or as part of a more generalized illness. A partial list of the more common microorganisms that can cause acute pharyngitis is presented in Table 29-1. Most cases of acute pharyngitis in children and adolescents are caused by viruses and are benign and self-limited. Group A beta-hemolytic streptococci (GAS) (*Streptococcus pyogenes*) is the most important of the bacterial causes of acute pharyngitis. Strategies for the diagnosis and treatment of pharyngitis in children and adolescents are directed at distinguishing the large group of patients with viral pharyngitis who would not benefit from antimicrobial therapy from the much smaller group of patients with GAS pharyngitis for whom antimicrobial therapy would be beneficial. Making this distinction is extremely important in attempting to minimize the unnecessary use of antimicrobial agents in children and adolescents.

TABLE 29-1. Etiology of Acute Pharyngitis

Etiologic Agent	Associated Disorder(s) or Clinical Findings(s)
Bacterial	
Streptococci	
Group A	Scarlet fever
Groups C and G	
Mixed anaerobes	Vincent angina
Neisseria gonorrhoeae	
Corynebacterium diphtheriae	Diphtheria
Arcanobacterium haemolyticum	Scarlatiniform rash
Yersinia enterocolitica	Enterocolitis
Yersinia pestis	Plague
Francisella tularensis	Tularemia (oropharyngeal form)
Viral	
Rhinovirus	Common cold
Coronavirus	Common cold
Adenovirus	Pharyngoconjunctival fever; acute respiratory disease
Herpes simplex virus types 1 and 2	Gingivostomatitis
Parainfluenza virus	Common cold; croup
Coxsackievirus A	Herpangina; hand, foot, and mouth disease
Epstein–Barr virus	Infectious mononucleosis
Cytomegalovirus	Cytomegalovirus mononucleosis
HIV	Primary HIV infection
Influenza A and B viruses	Influenza
Mycoplasmal	
Mycoplasma pneumoniae	Acute respiratory disease; pneumonia
Chlamydial	
Chlamydophila psittaci	Acute respiratory disease; pneumonia
Chlamydophila pneumoniae	Pneumonia

HIV, human immunodeficiency virus.
Modified from Bisno AL, Gerber MA, Gwaltney JM, et al. Practice guideline for the diagnosis and management of group A streptococcal pharyngitis. Clin Infect Dis 2002;35:113–125, with permission.

ETIOLOGY

Viruses are the most common cause of acute pharyngitis in children and adolescents. Respiratory viruses (e.g., influenza virus, parainfluenza virus, rhinovirus, coronavirus, adenovirus, and respiratory syncytial virus) are frequent causes of acute pharyngitis. Other viruses that frequently cause acute pharyngitis include coxsackievirus, echovirus, herpes simplex virus (HSV), and Epstein–Barr virus (EBV). The acute pharyngitis produced by EBV is often accompanied by other clinical findings of infectious mononucleosis (e.g., splenomegaly, generalized lymphadenopathy). Systemic infections with other viruses (e.g., cytomegalovirus, rubella virus, and measles virus) can be associated with acute pharyngitis.

GAS is the most common bacterial cause of acute pharyngitis, accounting for 15% to 30% of the cases of acute pharyngitis in children. Other bacteria that can cause acute pharyngitis include groups C and G beta-hemolytic streptococci and *Corynebacterium diphtheriae. Arcanobacterium haemolyticum* is a rare cause of acute pharyngitis in adolescents and *Neisseria gonorrhoeae* can cause acute pharyngitis in sexually active adolescents. Other bacteria such as *Francisella tularensis* and *Yersinia enterocolitica* as well as mixed infections with anaerobic bacteria (e.g., Vincent angina) are rare causes of acute pharyngitis. *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae* have been implicated as rare causes of acute pharyngitis, particularly in adults. Although other bacteria such as S*taphylococcus aureus*, *Haemophilus influenzae*, and *Streptococcus pneumoniae* are frequently isolated from throat cultures of children and adolescents with acute pharyngitis, their etiologic role in this illness has not been clearly established.

EPIDEMIOLOGY

Most cases of acute pharyngitis occur during the colder months of the year when respiratory viruses (e.g., rhinovirus, coronavirus, influenza virus, and adenovirus) are prevalent. Spread among family members in the home is a prominent feature of the epidemiology of most of these